BENZINDAZOLES BASED ON TRIKETONES OF THE INDAN SERIES

I. 5-Hydroxy-1-phenylbenz[g]indazoles

E. Ya. Ozola, A. K. Aren, and G. Ya. Vanag

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 2, pp. 331–334, 1969

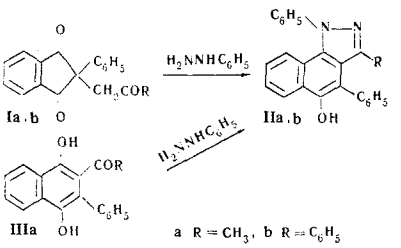
UDC 547.779'852.9:543.422.4.6

With phenylhydrazine, 2-acetonyl- and 2-phenacyl-2-phenylindan-1, 3-diones form phenylhydrazones at the carbonyl group of the side chain. On prolonged heating, a reaction takes place with the expansion of the five-membered ring into a six-membered ring and the formation of the corresponding 5-hydroxy-1-phenylbenz[g]indazoles. A reaction mechanism is proposed. The structure of the compounds obtained has been confirmed by their IR and UV spectra.

1,4-Diketones react with hydrazine and phenylhydrazine to form either dihydropyridazines or aminopyrroles [1–5], while sometimes the reaction is limited to the formation of mono- or dihydrazones of the initial diketones.

2,2-Disubstituted indan-1,3-diones containing an acetonyl or a phenacyl group in the 2 position are simultaneously 1,4-diketones. With the aim of obtaining cyclic nitrogenous compounds, we have studied the reaction of the 2-acetonyl- and 2-phenacyl-2-phenylindan-1,3-diones obtained previously [6, and 7, 8, respectively] with phenylhydrazine. As already established, 2,2-disubstituted indan-1,3-diones containing acetonyl and phenacyl groups in position 2 tend to expand the five-membered ring into a six-membered ring. Isomerization usually takes place when the triketones are heated with sodium methoxide in methanol, with the formation of 1,4-dihydroxynaphthalene derivatives [7, 9, 10].

It has been found that when 2-acetonyl- and 2-phenacyl-2-phenylindan-1,3-diones (**Ia** and **Ib**, respectively) are heated with phenylhydrazine in acetic acid, the five-membered ring of the indandione system again rearranges into a six-membered ring with the formation of derivatives of 5-hydroxy-1-phenylbenz-[g]indazole, **IIa, b**. The fact that the reaction does actually take place with the expansion of the ring is shown by the preparation of 5-hydroxy-3-methyl-1,4-diphenylbenz[g]indazole (**IIa**) directly from 3-acetyl-1,4-dihydroxy-2-phenylnaphthalene (**IIIa**) and phenylhydrazine when they are heated in glacial acetic acid. In all probability, the reaction takes place with the formation of the phenylhydrazone of the dihydroxynaphthalene **IIIa** which, on further heating, cyclizes into the benzindazole. The cyclization of cyclic β-ketoenols by means of phenylhydrazine has been described in the literature repeatedly. For example, 2-benzoyl-1-tetralone and its derivatives react with phenylhydrazine to form 1,3-diphenyl-4,5-dihydro-1H-benz[g]indazole [11, 12]. With phenylhydrazine, 2-benzoylnaphth-1-ol forms a phenylhydrazone which cyclizes in the presence of polyphosphoric acid to 1,3-diphenylbenz[g]indazole [13]. The cyclization of the phenylhydrazones of β-ketoenols has also been extended to derivatives of 3-acyl-4-hydroxycoumarins [14, 15].



However, the scheme given above for the independent synthesis of the hydroxybenzindazole derivative **IIa** from the corresponding dihydroxynaphthalene **IIIa**

Table 1

IR Spectra of the Phenylhydrazones **IV** and the Benzindazoles

Compound	Medium	ν in the 1500–1600 cm^{-1} region	$\nu_{C=N}$, cm^{-1}	$\nu_{C=O}$, cm^{-1}	$\nu_{NH,OH}$, cm^{-1}
2-Acetonyl-2-phenylindan-1,3-dione phenylhydrazone (**IVa**)	Nujol	1580, 1606		1712 1744	3333
2-Phenacyl-2-phenylindan-1,3-dione phenylhydrazone (**VIb**)	Nujol	1511, 1600		1709 1743	3333
5-Hydroxy-3-methyl-1,4-diphenylbenz[g]indazole (**IIa**)	Nujol	1505, 1585 1598	1620		
	Dichloroethane	1507, 1596	1625		3550
5-Acetoxy-3-methyl-1,4-diphenylbenz[g]indazole (**VIa**)	Nujol	1507, 1593		1761	
5-Acetoxy-1,3,4-triphenylbenz[g]indazole (**VIb**)	Nujol	1500, 1597		1773	

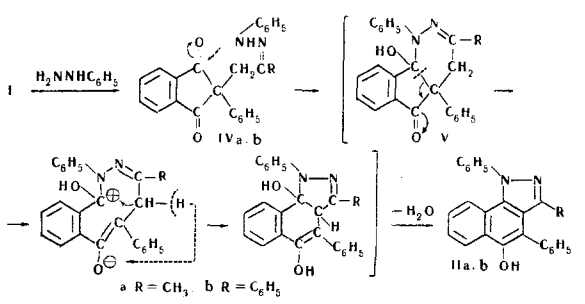
*The IR spectra were taken on a UR-10 instrument.

Table 2

UV Spectra of the Compounds Discussed in Ethanol

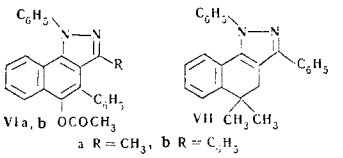
Compound	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)
Ia	227 (46.0)	250 Shoulder		
Ib	227 (45.2)	245 (32.0)		
IVa	226 (47.2)	268 (22.2)	300 Shoulder	
IVb	227 (45.0)	251 (20.2)	284 Shoulder	
IIa	221 (44.0)	266 (31.4)	320 (8.9)	342 (8.0)
IIb	220 (43.5)	258 (27.5)	320 (8.5)	340 (7.5)
		270 Shoulder		
VIa	224 (41.2)	257 (36.9)	301 (10.2)	340 (4.5)
VIb	222 (57.7)	252 (48.0)	310 (14.8)	342 (6.7)
VII		262 (22.4)	282 Shoulder	
			292 Shoulder	
			302 Shoulder	

gives no grounds for assuming that dihydroxynaphthalene derivatives are intermediates in the formation of benzindazole derivatives from the triketones **Ia, b**. The fact that the 2-acetonyl- and 2-phenacylindandiones **Ia, b**, form the phenylhydrazones **IVa, b** in acetic acid even at room temperature, compels one to imagine that the mechanism for the formation of the benzindazoles **II** from 2-acetonyl- and 2-phenacylindan-1, 3-diones is different from the mechanism of their formation from dihydroxynaphthalenes. In our opinion, the phenylhydrazones of the triketones **Ia, b** are intermediates in the reaction. Phenylhydrazine reacts with the carbonyl of the side chain since the IR spectra of the phenylhydrazones **IVa, b** retain the stretching vibrations of the β-dicarbonyl grouping (Table 1) [16]. Then, as a result of the intramolecular interaction of the amino and carbonyl groups of the phenylhydrazone, the polycyclic system of tetrahydropyridazine (**Va, b**) is formed, which then undergoes isomerization. The intermediate formation of the polycyclic system of tetrahydropyridazine is not a matter of doubt, since the intramolecular interaction of the amino and carbonyl groups leading to the polycyclic systems of pyrrolidine and pyrroline has been observed for aminoindandiones [17, 18]. Thus, it may be assumed that the process of rearrangement takes place within the tetrahydropyridazine derivative formed as an intermediate, and it can be represented by the following scheme:



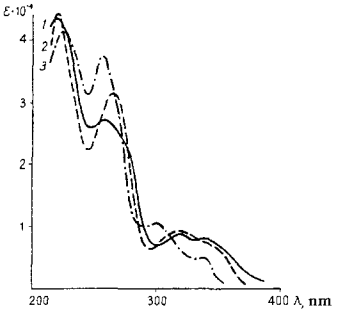
The driving force of the rearrangement of the indandione system into a benzoimidazole system is undoubtedly the gain in energy in the transfer from the intermediate system of the nonaromatic polycyclic tetrahydropyridazine to the aromatic system of benzindazole.

The 5-hydroxybenz[g]indazoles **IIa, b** that we obtained are colorless or slightly yellow substances soluble in ethanolic alkali with a yellow coloration. On acetylation they form the acetoxy derivatives **VIa, b**.



To confirm the structures put forward, the IR and UV spectra were recorded (Tables 1 and 2, respectively).

As already mentioned, the phenylhydrazones of the triketones **IVa, b** retain the characteristic frequencies of the stretching vibrations of the β-dicarbonyl grouping at 1710 and 1744 cm^{-1}. 5-Hydroxy-1, 3, 4-benz[g]-indazole has the band of the stretching vibrations of a hydroxy group at 3528 cm^{-1} in Nujol and at 3544 cm^{-1} in dichloroethane, while in 5-hydroxy-3-methyl-1, 4-diphenylbenz[g]indazole this band appears only in dichloroethane solution at 3550 cm^{-1} and is absent in Nujol, for some unknown reason. On acetylation, these frequencies disappear and the bands of the vibrations of an ester group appear in the 1760–1775 cm^{-1} region. In some compounds, low-intensity absorption appears at about 1625 cm^{-1}; we assume that this relates to the



UV absorption spectra:
1) **IIb**, 2) **IIa**, 3) **VIa**.

stretching vibrations of the C=N bond, since indazole and its derivative usually have a band of the vibrations of the C=N bond in the 1620–1660 cm^{-1} region [19].

stretching vibrations of the C=N bond in the 1620–1660 cm^{-1} region [19].

The UV spectra of the 5-hydroxybenz[g]indazoles (Table 2) have four absorption bands: strong bands at 220 and 260 nm and low-intensity bands at 320 and 342 nm. When the hydroxy group is acetylated, both the middle bands are shifted hypsochromically (see figure). For comparison, the absorption maxima of compound **VII**, which has been described in the literature [11], are given.

EXPERIMENTAL

2-Acetonyl-2-phenylindan-1,3-dione phenylhydrazone (IVa). A solution of 1.4 g (0.005 mole) of **Ia** in 6 ml of glacial acetic acid was treated with 1 ml (0.010 mole) of phenylhydrazine. After a few minutes, 1.65 g (89%) of **IVa** was filtered off in the form of yellow crystals with mp 209° C (from ethanol). Found, %: C 78.27; H 5.43; N 7.93. Calculated for $C_{24}H_{20}O_2N_2$, %: C 78.27; H 5.47; N 7.61.

2-Phenacyl-2-phenylindan-1,3-dione phenylhydrazone (IVb). A mixture of 3.4 g (0.01 mole) of **Ib** and 2.0 ml (0.02 mole) of phenylhydrazine was heated in 10 ml of glacial acetic acid for 7 min. A 3.1 g quantity (72%) of **IVb** deposited. It was recrystallized from ethanol to give yellow crystals with mp 207° C. Found, %: C 80.97; H 5.36; N 6.63. Calculated for $C_{28}H_{22}O_2N_2$, %: C 80.91; H 5.15; N 6.51.

5-Hydroxy-3-methyl-1,4-diphenylbenz[g]indazole (IIa). a) A mixture of 8.34 g (0.03 mole) of **Ia**, 5 ml (0.05 mole) of phenylhydrazine, and 35 ml of glacial acetic acid was heated for an hour. The solvent was distilled off, the residue was dissolved in 15–20 ml of ethanol, and the solution was left in the refrigerator. After 3 days, 5.3 g (50%) of **IIa** was filtered off. It was recrystallized from ethanol with the addition of activated carbon to give yellowish crystals with mp 170–171° C. The substance dissolves in ethanolic alkali with a yellowish coloration.

b) A mixture of 2.78 g (0.010 mole) of **IIIa**, 1.5 ml (0.015 mole) of phenylhydrazine, and 20 ml of glacial acetic acid was heated for 2 hr. The solvent was distilled off, and the oil was dissolved in ethanol and left in the refrigerator. After 4 days, 2.45 g (70%) of **IIa** was filtered off. Recrystallization from ethanol yielded slightly yellowish crystals with mp 170–171° C giving no depression of the melting point with the substance obtained in experiment (a). Found, %: C 81.98; H 5.21; N 8.28. Calculated for $C_{24}H_{18}ON_2$, %: C 82.28; H 5.18; N 8.00.

5-Hydroxy-1,3,4-triphenylbenz[g]indazole (IIb). A mixture of 3.4 g (0.010 mole) of **Ib**, 1.1 ml (0.011 mole) of phenylhydrazine, and 10 ml of glacial acetic acid was heated for 2 hr. On cooling, 3.16 g (77%) of **IIb** precipitated. Two crystallizations from acetic acid gave colorless crystals with mp 190–191° C. The substance dissolves in ethanolic alkali with a yellow coloration. Found, %: C 84.67; H 4.90; N 6.78. Calculated for $C_{29}H_{20}ON_2$, %: C 84.45; H 4.89; N 6.79.

5-Acetoxy-3-methyl-1,4-diphenylbenz[g]indazole (VIa). A mixture of 0.5 g of **IIa**, 10 ml of acetic anhydride, and 0.6 g of anhydrous sodium acetate was heated for an hour. The mixture was poured into water, and the precipitate was filtered off and recrystallized from ethanol, giving **VIa** in the form of colorless crystals with mp 195° C. Found, %: C 79.39; H 4.93; N 7.23. Calculated for $C_{26}H_{20}O_2N_2$, %: C 79.60; H 5.14; N 7.14.

5-Acetoxy-1,3,4-triphenylbenz[g]indazole (VIb). This was obtained from **IIb** in a similar manner to **VIa**. Colorless crystals with mp 178–179° C (from acetic acid). Found, %: C 81.81; H 4.99; N 6.16. Calculated for $C_{31}H_{22}O_2N_2$, %: C 81.89; H 4.88; N 6.17.

REFERENCES

1. C. Bülov and C. Sautermeister, Ber., **39**, 647, 1906.
2. A. Smith and H. N. McCoy, Ber., **35**, 2169, 1902.
3. C. Paal and E. Dencks, Ber., **36**, 491, 1903.
4. M. G. Korschun and C. Roll, Bull. Soc. chim. France, [4] **39**, 1223, 1926.
5. N. A. Domnin, M. N. Zelenina, and N. S. Glebovskaya, ZhOKh, **27**, 1516, 1957.
6. Gh. N. Gheorghiu, J. pr. Chem., **146**, 193, 1936.
7. E. Ya. Ozola and G. Ya. Vanag, Izv. AN Latv. SSR, ser. khim., 683, 1964.
8. F. M. Beringer and S. A. Galton, J. Org. Chem., **30**, 1930, 1965.
9. Gh. Gheorghiu, Bull. Soc. chim. France, [5] 6, 493, 1939.
10. E. Ya. Ozola and G. Ya. Vanag, ZhOrKh, **3**, 2201, 1967.
11. N. H. Cromwell, R. E. Bambury, and R. P. Barkley, J. Am. Chem. Soc., **81**, 4294, 1959.
12. N. H. Cromwell and R. E. Bambury, J. Org. Chem., **26**, 1729, 1961.
13. R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, Tetrah., **17**, 3, 1962.
14. N. S. Vul'fson and R. B. Zhurin, ZhOKh, **31**, 3381, 1961.
15. N. S. Vul'fson and R. B. Zhurin, ZhOKh, **32**, 991, 1962.
16. O. Neiland, in the collection: Cyclic β-Diketones [in Russian], Izd-vo AN Latv. SSR, Riga, p. 41, 1961.
17. G. Ya. Vanag and Ya. Ya. Dregeris, Izv. AN Latv. SSR. ser. khim., 559, 1964.
18. E. M. Danilova and V. V. Perekalin, ZhOrKh, **1**, 1708, 1965.
19. D. G. O'Sullivan, J. Chem. Soc., 3278, 1960.

22 December 1966

Institute of Organic Synthesis AS Latvian SSR, Riga